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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,133	02/28/2002	Sridhar Krishna Rabindran	ACY-33,316-D2	3539

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EXAMINER	
TRAVERS, RUSSELL S	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,133	RABINDRAN ET AL.	
	Examiner	Art Unit	
	Russell Travers, J.D.,Ph.D	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment and response filed January 15, 2004 have been received and entered into the file.

Applicant's arguments filed January 15, 2004 have been fully considered but they are not deemed to be persuasive.

Claims 64-69 are presented for examination.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, and thereby failing to provide an enabling disclosure.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth criteria allowing the skilled practitioner to identify those compounds that would provide a therapeutic benefit vis-a-vie "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells which exhibit non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", "test compound(s)", or chemotherapeutic agents required to practice the claimed invention. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of compounds useful as a "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", "test compound(s)", or chemotherapeutic agent examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring

each embodiment to be individually assessed for physiological activity. The instant claims read on all compounds which are a "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", any "test compound", or any chemotherapeutic agent, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Simply stated, the instant claims are an invitation to experiment for solutions to resistance experienced with chemotherapeutic regimens. The skilled artisan would respond to chemo-therapeutic failures by employing alternative drugs, or instituting concomitant administration of old and well known chemotherapeutic agents as taught by the Merck Manual. As herein claimed, and disclosed, the envisioned invention appears to be "a mere wish or plan for obtaining the claimed chemical invention" admonished by the Court of Appeals for the Federal Circuit in *Regents of the University of California v. Eli Lily & Co.* , (119 F3d 1559, 1566; USPQ2d 1398, 1406, (CAFC 1997), *cert denied,* 523 U.S. 089, 118 Sect. 1548 (1998)). To capture this subject matter Applicants are required to provide "a precise definition , such as by structure, formula, chemical name, or physical properties" of those compounds envisioned ((*Regents of the University of California v. Eli Lily & Co.*, *supra,* at 1566). Absent such information the instant claims fail to meet the enablement requirement set forth under 35 USC 112.

Claims 64-69 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 64-69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 64-69 are rendered indefinite by the phrases "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", a "chemosensitizing compound that reverses BCRP-mediated multiple drug resistance in cancer cells" and "test compound", and thereby failing to clearly set forth the metes and bounds of the patent protection desired. Criteria defining medicaments that are a "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells" or a "test compound" are not set forth in the specification, thereby failing to provide information defining the instant inventions metes and bounds. Applicant's terms fail to clearly define the subject matter encompassed by the instant claims, thus are properly rejected under 35 USC 112, second paragraph.

Claims 64-69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 64-69 are rendered indefinite by the phrases "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", those "chemosensitizing compound that reverses BCRP-mediated multiple drug resistance in cancer cells", a "test compound" and thereby failing to clearly set forth the subject matter of the patent protection desired. Examples of what "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", those "chemosensitizing compound that reverses BCRP-mediated multiple drug resistance in cancer cells", or those compounds effective as a "test compound" are not set forth in the specification. This failure additionally obscures any relationship between these compounds possibly envisioned for the instant invention. No clear relationship exists between a "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance in cancer cells" exhibiting non P-gp/non MRP drug resistance phenotype, "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", or "test compound(s)" recited in the instant claims. Absent exemplification, the skilled artisan could not establish the identity of compounds that could be envisioned as a "chemosensitizing compound that reverses non P-gp/non MRP multiple drug resistance" in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype, "chemosensitizing compounds that reverse

BCRP-mediated multiple drug resistance in cancer cells", or "test compound(s)". Applicant's phrases fail to clearly define the subject matter encompassed by the instant claims, thus is properly rejected under 35 USC 112, second paragraph.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 64-67 are rejected under 35 U.S.C. § 102(b) as being anticipated by Parekh et al.

Applicants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to preventing a malady or disease with old and well known compounds or compositions. It is now well settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex*

parte Novitski, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975).". In the instant application, Applicants' failure to distance the proffered claims from the anticipated prophylactic utility, renders such claims anticipated by the prior inherent use. Although the instant claims recite treating resistant neoplastic conditions with some unknown compound effecting some envisioned biochemical pathway, the instant recitation of mitoxantrone constructively admits by overcoming this resistance the prior art compound practices the claimed invention. Thus, the teaching of Parekh et al inherently practices the invention as recited.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 64-69 are rejected under 35 U.S.C. § 103 as being unpatentable over Parekh et al and Naito et al in view of the Merck Manual.

Parekh et al teach the various compounds, to include mitoxantrone herein claimed as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. This medicament is taught as useful for treating neoplastic diseases, the basis for resistance, taught as overcome, viewed by the skilled artisan as indistinguishable from those uses herein claimed. Naito et al teach resistance mediated by factors other than P-gp/MRP drug resistance phenotype. Attention is directed to Naito et al teaching over expression of the mRNA for this protein, yet no over expression of the protein, as herein envisioned. Examiner cited teachings disclosed the envisioned compounds, the resistance mechanisms herein envisioned, and those methods employed to ascertain resistance, rendering obvious those factors disclosed as a basis for the instant invention. Claims 64-69, and the primary references, differ as to:

1) the concomitant employment of these medicaments,

2) employing compounds concomitantly to provide therapy for resistant neoplasm's, and

3) recitation of inhibition levels.

It is generally considered prima facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of conventional anti-neoplastic agents. It would follow that the recited claims define prima facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 64-69 specifically require the addition of compounds concomitantly to neoplasms coupled with a determination of therapeutic effectiveness. Merck Manual teaches the treatment of neoplastic diseases as highly individual, with measures anti-neoplastic effectiveness as the goal of therapeutic success. Possessing Examiner□s teachings the skilled artisan would be motivated to employ the claimed compounds concomitantly and measure anti-neoplastic effectiveness. The skilled artisan would have seen administering the disclosed compounds concomitantly to overcome resistance as residing in the skilled artisan purview.

Claims 68-69 specifically require the addition of compounds which would provide therapeutic benefits for neoplastic diseases at levels greater than 22%. Parekh et al teaches the treatment of neoplastic diseases with anticancer agents that provide a therapeutic benefit in a dose dependant manner, while providing anti-neoplastic effectiveness as the goal of therapeutic success. Possessing Examiner's teachings the

skilled artisan would be motivated to employ the claimed compounds when observing resistance and measure anti-neoplastic effectiveness. The skilled artisan would have seen administering the disclosed compounds concomitantly, or individually to overcome resistance as residing in the skilled artisan purview.

RESPONSE TO ARGUMENTS

The Examiner notes the instant rejection under 35 USC 112, first and second paragraph result form a failure to place those specific compounds in the skilled artisan's possession. As stated above, attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the

monopoly asserted" *General Electric Company v. Wabash Appliance Corporation et* supra, at 468. Claims thus constructed provide no guidance as to medicaments employed, levels for providing therapeutic benefit, or provide notice for those practicing in the art, limits of protection. Simply stated, the presented claims are an invitation to experiment, not reciting a specific medicament regimen useful for practicing the instant invention.

Absent those compounds required to practice the instant invention, the metes and bounds for the instant claims are simply unknowable.

Newly presented rejections render the instant rebuttal arguments moot.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR

RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Travers, J.D.,Ph.D whose telephone number is 703-308-4603. The examiner can normally be reached on Monday to Thursday from 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-272-0631.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Travers J.D., Ph.D.
Primary Examiner
Art Unit 1617